Policy and Procedure	
PHARMACY PRIOR AUTHORIZATION POLICY AND CRITERIA ORPTCHEM029.1225	**HEMATOLOGICAL AGENTS THROMBOCYTOPENIA MEDICATIONS** See Table 1 for medications covered by policy
Effective Date: 3/1/2026	**Review/Revised Date**: 11/22, 11/23, 10/24, 10/25 (KN)
Original Effective Date: 02/22	**P&T Committee Meeting Date**: 12/21, 12/22, 12/23, 12/24, 12/25
Approved by: Oregon Region Pharmacy and Therapeutics Committee	

SCOPE:
Providence Health Plan and Providence Health Assurance as applicable (referred to individually as "Company" and collectively as "Companies").

APPLIES TO:
Commercial
Medicaid

POLICY CRITERIA:

COVERED USES:
All Food and Drug Administration (FDA)-Approved Indications, some medically accepted Indications.

REQUIRED MEDICAL INFORMATION:
For initiation of therapy, must meet indication-specific criteria below:

1. For **Oncologic Diagnoses:** Use must be for an FDA approved indication or indication supported by National Comprehensive Cancer Network guidelines with recommendation 2A or higher

2. For **Chemotherapy-Induced Thrombocytopenia (CIT)**, Nplate® may be covered if the following criteria are met:
   a. Platelet count of less than 100,000 cells per microliter
   b. One of the following:
      i. Thrombocytopenia for at least 3 weeks following the last chemotherapy administration
      ii. Thrombocytopenia resulting in delayed chemotherapy

3. For **Immune Thrombocytopenia (ITP),** Alvaiz®, Doptelet®, Nplate®, Promacta®, Tavalisse®, or Wayrilz® may be covered if the following criteria are met**:**
   a. Diagnosis of chronic immune thrombocytopenia (ITP)
   b. Platelet count of less than 30,000 cells per microliter

c. Treatment with at least one of the following therapies was ineffective or not tolerated, unless all are contraindicated:
    i. Systemic corticosteroids
    ii. Immune globulin
    iii. Splenectomy
d. For Alvaiz®, Doptelet®, Promacta®, or Tavalisse®: Inadequate response, intolerance, or contraindication to generic eltrombopag
e. For Wayrilz®: Inadequate response, intolerance, or contraindication to generic eltrombopag and Doptelet®

4. For **Chronic Hepatitis C-associated Thrombocytopenia**, Alvaiz® and Promacta® may be covered if the following criteria are met:
    a. Platelet count of less than 75,000 cells per microliter
    b. Patient will be initiating and maintaining interferon-based therapy or is currently receiving interferon-based therapy
    c. For Alvaiz® and Promacta®: Inadequate response, intolerance, or contraindication to generic eltrombopag

5. For **Severe Aplastic Anemia**, Alvaiz® and Promacta® may be covered if both of the following criteria are met:
    a. Platelet count of less than 30,000 cells per microliter
    b. Requested medication must be used in combination with standard immunosuppressive therapy (antithymocyte globulin [ATG] plus cyclosporine) OR has tried and had an insufficient response to immunosuppressive therapy
    c. For Alvaiz® and Promacta®: Inadequate response, intolerance, or contraindication to generic eltrombopag

6. For **Treatment of Thrombocytopenia in Patients with Chronic Liver Disease (CLD)**, Doptelet® or Mulpleta® may be covered if the following criteria is met**:**
    a. Diagnosis of chronic liver disease
    b. Platelet count of less than 50,000 cells per microliter
    c. Patient will have a scheduled medical or dental procedure within the next 30 days
    d. For Mulpleta®: Documented trial, failure, intolerance, or contraindication to Doptelet®

7. For **Hematopoietic Syndrome of Acute Radiation Syndrome [HSARS]**, Nplate® may be covered if patient has suspected or confirmed exposure to radiation levels greater than 2 gray (Gy)

8. For **acquired Thrombotic Thrombocytopenic Purpura (aTTP)**, Cablivi may be covered if both of the following criteria are met:

a. Documentation that therapy will be given in combination with plasma exchange therapy
b. Documentation that therapy will be given in combination with immunosuppressive therapy (such as glucocorticoids, rituximab)

For patients established on therapy, must meet indication-specific criteria below:

1. For **oncologic diagnoses, ITP, and severe aplastic anemia:** Improved platelet levels from baseline

2. For **Chemotherapy-Induced Thrombocytopenia (CIT)**:
    a. Improved platelet count from baseline
    b. Attestation that patient requires medication to continue receiving chemotherapy

3. For **Chronic Hepatitis C-associated Thrombocytopenia:**
    a. Improved platelet levels from baseline
    b. Patient continues to receive interferon-based therapy

4. For **CLD or HSARS**: Patient must meet the initial approval criteria above for each request

5. For **aTTP**:
    a. Documentation of previous positive response to therapy (such as an improvement in platelet counts, reduction in neurological symptoms, or improvements in organ-damage markers)
    b. Documentation that length of therapy post plasma exchange will not exceed 58 days
    c. If the request is for a new treatment cycle:
        i. Documentation that therapy will be given in combination with plasma exchange therapy and immunosuppressive therapy (such as glucocorticoids, rituximab)
        ii. Documentation that patient has not had more than two recurrences of acquired thrombotic thrombocytopenic purpura while on therapy with caplacizumab. Recurrence is defined as initial platelet normalization followed by a reduction in platelet count that necessitates re-initiation of plasma exchange.
    d. If request is for treatment extension:
        i. Documentation that patient has signs of persistent underlying disease such as persistent severe ADAMTS13 deficiency (less than 10% or 10 IU/dL)

EXCLUSION CRITERIA:

Concomitant use with other thrombopoietin receptor agonists (e.g., Mulpleta®, Promacta®, Nplate®) or with tyrosine kinase inhibitors (e.g., Tavalisse®).

AGE RESTRICTIONS:
Age must be appropriate based on FDA-approved indication

PRESCRIBER RESTRICTIONS:
Must be prescribed by, or in consultation with, an oncologist, hematologist, gastroenterologist or hepatologist.

COVERAGE DURATION:
- For **ITP, chemotherapy-induced thrombocytopenia (CIT), chronic hepatitis C-associated thrombocytopenia, severe aplastic anemia,** and **oncologic diagnoses**: Initial authorization will be approved for six months. Reauthorization will be approved for one year
- For **CLD**: Authorization will be approved for one month for one treatment course
- For **HSARS**: Authorization will be approved for three months
- For **aTTP**: Initial authorization will be approved for 30 days. Reauthorization will be approved up to a total duration of 58 days post-plasma-exchange

QUANTITY LIMIT:
Cablivi®: one vial per day
Doptelet®: fifteen tablets per 30 days
Mulpleta®: seven tablets per 30 days
Promacta®:
- 12.5 mg tablets, 12.5 mg powder packets, 25 mg tablets: one tablet/packet per day
- 50 mg and 75 mg tablets: two tablets per day
- 25 mg powder packets: six packets per day

Tavalisse®: two tablets per day
Wayrilz®: two tablets per day

Requests for indications that were approved by the FDA within the previous six (6) months may not have been reviewed by the health plan for safety and effectiveness and inclusion on this policy document. These requests will be reviewed using the New Drug and or Indication Awaiting P&T Review; Prior Authorization Request ORPTCOPS047.

Requests for a non-FDA approved (off-label) indication requires the proposed indication be listed in either the American Hospital Formulary System (AHFS), Drugdex, or the National Comprehensive Cancer Network (NCCN) and is considered subject to evaluation of the prescriber's medical rationale, formulary alternatives, the available published evidence-based research and whether the proposed use is determined to be experimental/investigational.

Coverage for Medicaid is limited to a condition that has been designated a covered line item number by the Oregon Health Services Commission listed on the Prioritized List of Health Care Services.

Coverage decisions are made on the basis of individualized determinations of medical necessity and the experimental or investigational character of the treatment in the individual case.

INTRODUCTION:

Thrombocytopenia is a condition characterized by a low blood platelet count. Platelets (thrombocytes) are colorless blood cells that help blood clot. Thrombopoietin receptor agonists (TPO-RAs; e.g., Mulpleta®, Promacta®, Nplate®, Alvaiz®), spleen tyrosine kinase (SYK) inhibitors (e.g., Tavalisse®), and bruton tyrosine kinase (BTK) inhibitors (e.g., Wayrilz®) are medications used to treat thrombocytopenia when standard therapies, such as corticosteroids, are not sufficient. TPO-RAs increase the production of platelets by stimulating bone marrow cells, whereas the SYK inhibitors work by preventing the breakdown of platelets. The BTK, Wayrilz®, works by reducing autoantibody signaling, blocking B cell signaling, and decreasing autoantibody generation through effects on B cell activation.

Caplacizumab-yhdp injection (Cablivi®) is a monoclonal antibody that targets the A1 domain of von Willebrand factor (vWF) and inhibits the interaction between vWF and platelets, thus reducing platelet adhesion and consumption. It is the first targeted treatment for acquired thrombotic thrombocytopenic purpura (aTTP).

FDA APPROVED INDICATIONS:

Table 1

Brand (generic)	FDA indications
Alvaiz® (eltrombopag) tablet	• Treatment of thrombocytopenia in adult and pediatric patients 6 years and older with persistent or chronic immune thrombocytopenia (ITP) who have had an insufficient response to corticosteroids, immunoglobulins, or splenectomy • Treatment of thrombocytopenia in adult patients with chronic hepatitis C to allow the initiation and maintenance of interferon-based therapy • Treatment of adult patients with severe aplastic anemia who have had an insufficient response to immunosuppressive therapy
Cablivi® (caplacizumab-yhdp) injection	• Treatment of adult patients with acquired thrombotic thrombocytopenic purpura (aTTP), in combination with plasma exchange and immunosuppressive therapy
Doptelet® (avatrombopag) tablet	• Treatment of thrombocytopenia in adult patients with chronic liver disease who are scheduled to undergo a procedure • Treatment of thrombocytopenia in adult patients with chronic immune thrombocytopenia who have had an insufficient response to a previous treatment

	• Treatment of thrombocytopenia in pediatric patients 1 year and older with persistent or chronic thrombocytopenia who have had an insufficient response to a previous treatment
Mulpleta® (lusutrombopag) tablet	• Treatment of thrombocytopenia in adult patients with chronic liver disease who are scheduled to undergo a procedure
Nplate® (romiplostim) SQ injection	• Pediatric patients one year of age and older with immune thrombocytopenia (ITP) for at least six months who have had an insufficient response to corticosteroids, immunoglobulins, or splenectomy. • Adults with immune thrombocytopenia (ITP) who have had an insufficient response to corticosteroids, immunoglobulins, or splenectomy. • To increase survival in adults and in pediatric patients (including term neonates) acutely exposed to myelosuppressive doses of radiation (Hematopoietic Syndrome of Acute Radiation Syndrome [HSARS]).
Promacta® (eltrombopag olamine) tablets/packet	• Treatment of thrombocytopenia in adult and pediatric patients 1 year or older with persistent or chronic immune thrombocytopenic purpura (ITP) who have had an insufficient response to corticosteroids, immunoglobulins, or splenectomy. Promacta should be used only in patients with ITP whose degree of thrombocytopenia and clinical condition increase the risk for bleeding. • Treatment of thrombocytopenia in patients with chronic hepatitis C to allow the initiation and maintenance of interferon-based therapy. Promacta should be used only in patients with chronic hepatitis C whose degree of thrombocytopenia prevents the initiation of interferon-based therapy or limits the ability to maintain interferon-based therapy. • Patients with severe aplastic anemia who have had an insufficient response to immunosuppressive therapy. • In combination with standard immunosuppressive therapy for the first-line treatment of adult and pediatric patients two years and older with severe aplastic anemia.
Tavalisse® (fostamatinib disodium) tablet	Treatment of thrombocytopenia in adult patients with chronic immune thrombocytopenia (ITP) who have had an insufficient response to a previous treatment.
Wayrilz® (rilzabrutinib) tablet	Treatment of adult patients with persistent or chronic immune thrombocytopenia (ITP) who have had an insufficient response to a previous treatment

POSITION STATEMENT:

Immune Thrombocytopenia (ITP)

ITP is an autoimmune disorder characterized by isolated thrombocytopenia (low blood platelet count) with an otherwise normal complete blood count in the absence of other apparent causes (i.e., associated conditions, drugs). The main clinical manifestations of ITP are related to excessive bleeding, which is typically mucocutaneous including petechiae, purpura, easy bruising, epistaxis, gingival bleeding, and menorrhagia. More overt bleeds such as gastrointestinal bleeds, gross hematuria, and intracranial hemorrhage are rare.[2]

The American Society of Hematology (ASH) 2019 guidelines recommend short courses of corticosteroids (less than or equal to six weeks) as first-line treatment. Intravenous immunoglobulin (IVIG) either as single agent or in combination with corticosteroids may also be appropriate. Second-line treatments include splenectomy, TPO-receptor agonists (e.g., eltrombopag, romiplostim), and rituximab. Splenectomy is the only treatment that provides sustained remission for at least one year in a high proportion of ITP patients. The goal in treatment of ITP is not to achieve a normal platelet count but a safe level that avoids bleeding.[2]

Chronic Hepatitis C-associated Thrombocytopenia

Thrombocytopenia in chronic hepatitis C virus (HCV) infection is a significant issue, especially in patients with advanced disease. It can prevent the use of invasive biopsies for staging, complicate bleeding manifestations, and impede the use of antiviral therapy. Thrombocytopenia results from the autoimmune reaction (anti-platelet antibodies) as well as direct bone marrow suppression caused by the virus.[3]

Eradicating the virus is an important step in treating thrombocytopenia. With interferon-based antiviral therapy, HCV treatment is typically continued with a dose reduction if platelets decrease below 50,000 cells/mcl and discontinued for platelets below 25 x 10^9/L. Thrombopoietin (TPO) is a cytokine that plays a central role in thrombopoiesis by activating cascades which result in the proliferations and maturation of megakaryocytes. TPO-mimetic agents, such as eltrombopag and romiplostim, have shown benefit in treating thrombocytopenia without inducing an immune response.[3]

Severe Aplastic Anemia

Aplastic anemia (AA) is a disorder of stem cell failure, leading to pancytopenia (a reduction of all types of blood cells) in the absence of splenomegaly. Affected patients may present with recurrent infections, uncontrolled bleeding and feeling fatigued. AA can be temporary or permanent and causes may include, but are not limited to, radiation and chemotherapy, drug adverse effects, viral infection, or pregnancy.[4]

The British Society for Haematology 2024 guidelines therapeutic strategy for severe AA includes allogeneic hematopoietic cell transplant (HCT) and for non-transplant candidates, immunosuppressive therapy (combined use of anti-thymocyte globulin and cyclosporine) as first-line treatment. Eltrombopag is recommended as an add on treatment for first-line therapy or when standard first-line immunosuppressive therapy has failed.[4]

Hematopoietic Syndrome of Acute Radiation Syndrome (HSARS)
Hematopoietic Syndrome of Acute Radiation Syndrome (HSARS) occurs in adult and pediatric patients exposed to myelosuppressive doses of radiation. Symptoms include nausea, vomiting, diarrhea, headache, weakness, or drop in blood counts. Romiplostim is a synthetic thrombopoietin (TPO) receptor agonist which may be used to treat this syndrome by increasing the generation of platelets within the bone marrow.[5]

Thrombocytopenia in adult patients with Chronic Liver Disease (CLD)
Thrombocytopenia is a common complication in patients with chronic liver disease. Patients with that moderate thrombocytopenia (platelet counts between 50-75 x 10^9/L) can often be asymptomatic and typically do not have an increased risk of bleeding during procedures. However, severe thrombocytopenia (platelet count less than 50 x 10^9/L) is associated with increased risk of morbidity and these patients can experience serious bleeding and have other complications when undergoing certain procures or surgical interventions. TPO-receptor agonists, such as the first-generation eltrombopag and second generation avatrombopag and lusutrombopag, work at a different locus on the TPO receptor than the endogenous TPO, resulting in a synergistic effect in increasing the production of platelets and the maturation of megakaryocytes.[6]

Acquired Thrombotic thrombocytopenia purpura (aTTP)
Thrombotic thrombocytopenia purpura (TTP) is a rare blood disorder, characterized by blood clots that form in small blood vessels which can cause thrombocytopenia, hemolytic anemia, and organ damage. TTP is caused by severely reduced activity of the von Willebrand factor-cleaving protease ADAMTS13 (<10% or 10 IU/dL) which leads to an accumulation of vWF multimers and induces platelet aggregation. Two main types of TTP are inherited TTP due to inherited mutations in the ADAMTS13 gene and acquired TTP due to the development of autoantibodies against ADAMTS13. ATTP occurs in approximately three adults per one million per year, mean age of 41. Symptoms include fatigue, dyspnea, petechiae, or other bleeding but these symptoms may not present until the condition is severe. The standard of care treatment approach in aTTP involves the initiation of plasma exchange to remove autoantibodies and replenish ADAMTS13, in addition to immunosuppressive therapy (glucocorticoids and rituximab) to inhibit autoantibody formation. However,

even with current treatments, the risk remains for thrombotic complications, exacerbations, and death.

In the phase 3 HERCULES trial treatment, caplacizumab, in combination with plasma exchange and immunosuppression, resulted in a significantly shorter time to platelet count response vs. plasma exchange and immunosuppression alone (Hazard Ratio = 1.55 [95% CI: 1.10, 2.20]; p = 0.01). Additionally, the caplacizumab group saw a significant reduction in the composite endpoint of aTTP-related death, recurrence of aTTP, or a major thromboembolic event during study drug treatment vs. placebo (12.7% vs. 49.3%; p < 0.0001). The safety and efficacy of caplacizumab was also assessed in the phase 2 TITAN trial. These trials provide a moderate quality of evidence that caplacizumab may produce clinically meaningful outcomes in patients with acquired TTP that require plasma exchange.

Guidelines from the International Society of Thrombosis and Haemostasis suggest using caplacizumab over not using it for first or relapsing episodes of aTTP. They state the drug should only be used by clinicians with experience in both the medication and treatment of TTP. While caplacizumab can be started while awaiting the results of plasma ADAMTS13 activity, caplacizumab therapy should be stopped if the results show ADAMTS13 activity greater than 20% (or 20 IU/DL) which constitutes a negative result for TTP. Stopping caplacizumab after platelet normalization but if ADAMTS13 activity still low (<10% or 10 IU/dL) may result in disease exacerbation. Immunosuppressive therapies such as corticosteroids and rituximab should be continued to help control the underlying disease processes.[7]

Dosing and administration:
Caplacizumab should be administered upon initiation of plasma exchange therapy and the recommended dose of caplacizumab is as follows:

- First day of treatment: 11 mg bolus intravenous injection at least 15 minutes prior to plasma exchange followed by an 11 mg subcutaneous (SC) injection after completion of plasma exchange on day one
- Subsequent days of treatment during daily plasma exchange: 11 mg SC injection once daily following plasma exchange
- Treatment after plasma exchange period: 11 mg SC injection once daily continuing for 30 days following the last daily plasma exchange. If, after the initial treatment course, signs of persistent underlying disease such as suppressed ADAMTS13 activity levels (<10% or 10 IU/dL) remain present, treatment may be extended for a maximum of 28 days (for a total of 58 days after plasma exchange discontinuation)
- Caplacizumab should be discontinued if the patient experiences more than two recurrences of aTTP, while on caplacizumab

BILLING GUIDELINES AND CODING for medically administered medications within this policy:

HCPCS	Coding Description	Brand Name
Medical Benefit		
J2802	Injection, romiplostim, 1 microgram	NPLATE
C9047	Injection, caplacizumab-yhdp, 1 mg	Cablivi
Pharmacy Benefit		
J8499	Prescription drug, oral, non chemotherapeutic, nos	Alvaiz, Doptelet Mulpleta Promacta Wayrilz
ADMINISTRATION CODES◊		
96372	Ther/proph/diag inj sc/im	
96374	Ther/proph/diag inj iv push	
96401	Chemo anti-neopl sq/im	
96409	Chemo iv push sngl drug	

◊ Coding/Administration Notes:
• The above code list is provided as a courtesy and may not be all-inclusive. Inclusion or omission of a code from this policy neither implies nor guarantees reimbursement or coverage. Some codes may not require routine review for medical necessity, but they are subject to provider contracts, as well as member benefits, eligibility and potential utilization audit.
• HCPCS/CPT code(s) may be subject to National Correct Coding Initiative (NCCI) procedure-to-procedure (PTP) bundling edits and daily maximum edits known as "medically unlikely edits" (MUEs) published by the Centers for Medicare and Medicaid Services (CMS). This policy does not take precedence over NCCI edits or MUEs. Please refer to the CMS website for coding guidelines and applicable code combinations.

REFERENCE/RESOURCES:

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